QUIDEL®
CORPORATION

MAR 8 2013

510(k) SUMMARY

510(k) Number:
k123998 - Quidel Molecular Direct C. difficile Assay

Date of Preparation:
December 20, 2012

Submitted by:
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Proprietary and Established Names:
Quidel Molecular Direct C. difficile Assay

Common Name:
Clostridium difficile Nucleic Acid Test
C. difficile assay
C. diff test

Regulatory Information:
Regulation section: 21 CFR 866.3130 - C. difficile Nucleic Acid Amplification Test Assay
Classification: II
Product code: OZN - Amplification assay for the detection of *Clostridium difficile* toxin genes from stool specimens of symptomatic patients
Panel: Microbiology (83)

Predicate Devices:
Portrait Toxigenic C. difficile Assay (K113358) (Great Basin Scientific)

510(k) Summary: Quidel Molecular Direct C. difficile Assay

Intended Use:

The Quidel Molecular Direct C. difficile Assay is a qualitative, multiplexed *in vitro* diagnostic test for the direct detection of toxin A gene (*tcdA*) or toxin B gene (*tcdB*) sequences of toxigenic strains of *Clostridium difficile* from unformed (liquid or soft) stool specimens collected from patients suspected of having *Clostridium difficile*-Associated Disease (CDAD).

The Quidel Molecular Direct C. difficile Assay is a real-time PCR test and utilizes proprietary sample preparation with fluorescently labeled primers and probes. The assay can be performed using either the Life Technologies QuantStudio® Dx; the Applied Biosystems 7500 Fast Dx, or the Cepheid SmartCycler II, to detect the toxin gene sequences associated with toxin-producing *C. difficile* strains.
The assay is intended to be performed directly on CDAD-suspected stool specimens, and is indicated for use as an aid in the diagnosis of CDAD.

Special instrument requirements:
Life Technologies QuantStudio® Dx software version 1, or
Applied Biosystems 7500 Fast Dx software version 1.4, or
Cepheid SmartCycler II software version 3.0b

Device Description:

The Quidel Molecular Direct C. difficile Assay detects nucleic acids that have been prepared from a patient sample using proprietary sample preparation. A multiplex real-time PCR reaction is performed under optimized conditions in a single well generating amplicons for each of the targets present in the sample. Identification occurs by the use of oligonucleotide primers and probes that are complementary to conserved regions in the *tcdA* and *tcdB* genes of the pathogenicity locus (PaLoc).

The Quidel Molecular Direct C. difficile Assay contains sufficient reagents to process 96 specimens or quality control samples. The kit contains the following:

SKU # M105
Assay Kit (96 Reactions) – Store at 2° to 8°C

#	Component	Quantity
❶	Rehydration Solution Part M5003	1 vial/kit 1.9 mL
❷	Quidel Molecular C. difficile Master Mix Part M5043	12 vials/kit 8 reactions/vial

SKU # M207
Rapid DNA Stool Sample Prep Kit (96 Specimens) – Store at 2° to 25°C

#	Component	Quantity
❶	Process Buffer 1 Part M5032	96 tubes/kit 500 µL

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#	Component	Quantity
❷	Process Buffer 2 Part M5033 Contains Process Control	96 tubes/kit 570 µL
	Neonatal flocked Swabs Part M5034	96 swabs

Test Principle:

The Quidel Molecular Direct C. difficile Assay detects nucleic acids that have been prepared from a patient sample using proprietary sample preparation. A multiplex real-time PCR reaction is performed under optimized conditions in a single well generating amplicons for each of the targets present in the sample. Identification occurs by the use of oligonucleotide primers and probes that are complementary to conserved regions in the *tcdA* and *tcdB* genes of the pathogenicity locus (PaLoc).

The following is a summary of the procedure:

1. **Sample Collection:** Dip a neonatal flocked swab into the liquid or soft stool specimen using standard techniques from pediatric and adult patients suspected of having Clostridium difficile-Associated Disease (CDAD).
   Note: Remove mucus from the specimen prior to sampling the fecal material.

2. **Sample Preparation:** Twirl the neonatal flocked swab in the first process buffer then add 30 µL of the sample into the second process buffer tube which contains the process control (PRC).

3. **Rehydration of Master Mix:** Rehydrate the lyophilized Master Mix using the Rehydration Solution. The Master Mix contains oligonucleotide primers, fluorophore and quencher-labeled probes targeting conserved regions of the *tcdA* and *tcdB* as well as the process control sequence.

4. **Nucleic Acid Amplification and Detection:** Add 15 µL of the rehydrated Master Mix to each reaction tube or plate well. Then add 5 µL of prepared specimen (specimen with PRC) to the plate well or appropriately labeled reaction tube. Place the plate or tube into the Life Technologies QuantStudio® Dx, Applied Biosystems 7500 Fast Dx instrument or Cepheid® SmartCycler® II instruments.

Once the reaction tube or plate is added to the instrument, the Quidel Molecular Direct C. difficile Assay protocol is initiated. This assay is based on Taqman® chemistry, and uses an enzyme with DNA polymerase, and 5'-3' exonuclease activities. During DNA amplification, this enzyme cleaves the probe bound to the complementary DNA sequence, separating the quencher

dye from the reporter dye. This step generates an increase in fluorescent signal upon excitation by a light source of the appropriate wavelength. With each cycle, additional dye molecules are separated from their quenchers resulting in an increase in the fluorescent signal. If sufficient fluorescence is achieved, the sample is reported as positive for the detected nucleic acid.

Performance Characteristics

Analytical performance:

Detection limit: The analytical sensitivity (limit of detection or LoD) of the Quidel Molecular Direct C. difficile Assay was determined on each instrument using quantified (CFU/mL) cultures of two *C. difficile* strains (ATCC BAA-1870 and ATCC BAA-1872) serially diluted in a negative fecal matrix. Analytical sensitivity (LoD) is defined as the lowest concentration at which 95% of all replicates tested positive.

Applied Biosystems 7500 Fast Dx

Strain Designation	Toxinotype	Calculated CFU/mL at LoD	CFU per Assay at LoD	LoD Confirmation Results
ATCC BAA-1870	IIIb	8.4E+04	4.2E-01	60/60
ATCC BAA-1872	0	2.4E+04	1.2E-01	59/60

Life Technologies QuantStudio

Strain Designation	Toxinotype	Calculated CFU/mL at LoD	CFU per Assay at LoD	LoD Confirmation Results
ATCC BAA-1870	IIIb	8.4E+04	4.2E-01	20/20
ATCC BAA-1872	0	8.0E+03	4.0E-02	20/20

Cepheid SmartCycler II

Strain Designation	Toxinotype	Calculated CFU/mL at LoD	CFU per Assay at LoD	LoD Confirmation Results
ATCC BAA-1870	IIIb	8.4E+04	4.2E-01	58/60
ATCC BAA-1872	0	2.4E+04	1.2E-01	60/60

The final assay LoD is defined as the higher of the two strain concentrations where 95% positivity was observed. The final assay LoD is 4.2E-01 CFU/assay.

510(k) Summary: Quidel Molecular Direct C. difficile Assay

Analytical Reactivity (Inclusivity): Twenty-four toxigenic strains for *C. difficile* were tested at 2 to 3x LoD in negative specimen matrix using three (3) Quidel Molecular Direct C. difficile Assay lots. Strains were reported to originate from at least five states and four countries (USA, Belgium, France and Sweden). Seven (7) toxinotypes were represented: 0, IIIb, IIIc, IV, V, VIII and XXIII. The analytical reactivity (inclusivity) testing conducted demonstrated that the Quidel Molecular Direct C. difficile Assay can detect a broad range of toxigenic *Clostridium difficile* strains at 2 to 3x LoD.

Analytical specificity:

Cross-Reactivity

The analytical specificity of the Quidel Molecular Direct C. difficile Assay was evaluated by testing a panel consisting of 66 bacterial, viral and yeast microorganisms and human DNA representing common enteric pathogens, flora or nucleic acid commonly present in the intestine. Microorganisms or nucleic acid was mixed with pooled negative matrix and tested directly or in the presence of 2 to 3x LoD level of *C. difficile* for cross reactivity and microbial interference, respectively. Bacteria were tested at concentrations greater than 1.0E+06 CFU/mL and viruses at greater than 1.0E+05 PFU/mL. In addition, *in silico* analysis showed that the Quidel Molecular Direct C. difficile Assay had no predicted cross-reactivity for *C. botulinum*. The results of this study demonstrate that the Quidel Molecular Direct C. difficile Assay does not cross-react with medically relevant levels of viruses or bacteria found in stool specimens.

Interfering Substances

Two toxigenic strains of *C. difficile* (ATCC BAA-1870 and ATCC BAA-1872) were evaluated against a test panel consisting of thirty-five substances found in stool specimens. Substances were introduced into the assay dilution tubes at concentrations which were medically relevant. Each of the strains was tested for each substance. None of the substances tested were found to interfere with the Quidel Molecular Direct C. difficile Assay.

Precision/Reproducibility:

Precision:

For the Precision/Within Laboratory Repeatability study, a blinded four-member panel consisting of *C. difficile* positive and negative sample was tested by two operators, twice a day using a single assay lot of Quidel Molecular Direct C. difficile Assay for twelve (12) days on all three instruments.

510(k) Summary: Quidel Molecular Direct C. difficile Assay

Applied Biosystems 7500 Fast Dx				
C. difficile	5X LoD	2X LoD	0.3X LoD	Negative
% Detection	100%	100%	71%	0%
Average Ct	18.2	20.5	25.8	N/A
STDEV	1.0	1.3	2.4	N/A
%CV	5.2%	6.2%	9.4%	N/A

Life Technologies QuantStudio™ Dx Real-Time PCR Instrument				
C. difficile	5X LoD	2X LoD	0.3X LoD	Negative
% Detection	100%	100%	88%	0%
Average Ct	16.51	17.70	21.13	N/A
STDEV	0.42	0.76	1.37	N/A
%CV	2.6%	4.3%	6.5%	N/A

Cepheid SmartCycler II				
C. difficile	5X LoD	2X LoD	0.3X LoD	Negative
% Detection	100%	96%	27%	0%
Average Ct	18.3	20.6	23.6	N/A
STDEV	1.1	1.3	1.1	N/A
%CV	6.0%	6.4%	4.7%	N/A

Reproducibility:

In order to confirm the reproducibility of the Quidel Molecular Direct C. difficile Assay a blinded and randomized study panel containing *Clostridium difficile* negative and positive samples were tested at three (3) test sites, two of which were clinical sites. Each site tested a reproducibility panel and assay controls for five (5) days in triplicate on each instrument. The testing was done by two operators at each site. Each operator ran the panel once a day using one lot of Quidel Molecular Direct C. difficile Assay.

Reproducibility Results – Applied Biosystems 7500 Fast Dx										
Panel Member ID	Site 1			Site 2			Site 3			Total Results
	Results	AVE Ct	%CV	Results	AVE Ct	%CV	Results	AVE Ct	%CV	
High Negative 0.3x LoD	5/29	28.8	15.0	11/30	27.1	9.0	16/30	27.6	2.8	32/89
Low Positive 2x LoD	29/30	23.2	8.4	30/30	22.7	7.5	29/30	23.1	6.5	88/90
Med Positive 5x LoD	30/30	20.5	5.7	30/30	20.2	5.0	30/30	20.4	5.0	90/90
Negative Specimen	0/29	N/A	N/A	0/30	N/A	N/A	0/30	N/A	N/A	0/89
Negative Control	0/30	N/A	N/A	0/30	N/A	N/A	0/30	N/A	N/A	0/90
Positive Control	30/30	15.8	2.9	30/30	16.2	2.6	30/30	15.7	2.9	90/90

Reproducibility Results – Life Technologies QuantStudio Dx										
Panel Member ID	Site 1			Site 2			Site 3			Total Results
	Results	AVE Ct	%CV	Results	AVE Ct	%CV	Results	AVE Ct	%CV	
High Negative 0.3x LoD	8/30	22.9	5.0	15/30	22.5	5.7	15/30	22.5	1.5	38/90
Low Positive 2x LoD	30/30	20.4	5.9	30/30	19.0	5.1	30/30	19.2	0.8	90/90
Med Positive 5x LoD	30/30	18.4	4.2	30/30	17.5	2.2	30/30	17.9	0.7	90/90
Negative Specimen	0/30	N/A	N/A	0/30	N/A	N/A	0/30	N/A	N/A	0/90
Negative Control	0/30	N/A	N/A	0/30	N/A	N/A	0/30	N/A	N/A	0/90
Positive Control	30/30	15.7	0.6	30/30	15.7	0.1	30/30	15.5	0.1	90/90

Reproducibility Results – Cepheid SmartCycler II										
Panel Member ID	Site 1			Site 2			Site 3			Total Results
	Results	AVE Ct	%CV	Results	AVE Ct	%CV	Results	AVE Ct	%CV	
High Negative 0.3x LoD	17/30	23.4	6.6	22/30	25.3	13.4	26/30	23.4	9.3	65/90
Low Positive 2x LoD	29/30	20.1	4.6	29/29	20.1	5.1	30/30	19.9	6.4	88/89
Med Positive 5x LoD	30/30	18.4	9.5	30/30	18.5	3.1	30/30	18.3	6.4	90/90
Negative Specimen	0/30	N/A	N/A	0/30	N/A	N/A	0/29	N/A	N/A	0/89
Negative Control	0/30	N/A	N/A	0/30	N/A	N/A	0/29	N/A	N/A	0/89
Positive Control	30/30	15.1	3.8	30/30	14.8	2.2	30/30	14.5	3.4	90/90

Clinical performance:

The performance of the Quidel Molecular Direct C. difficile Assay was evaluated with specimens collected at four geographically diverse locations within the United States between August 2012 and November 2012. In two studies (one study for the ABI 7500 Fast Dx and Cepheid SmartCycler II (665 specimens) and a second study for the QuantStudio Dx (792 specimens)), the Quidel Molecular Direct C. difficile Assay was compared to cytotoxic tissue culture and an enriched toxigenic *C. difficile* culture. The tables below present the data from these studies.

Applied Biosystems 7500 Fast Dx

Performance characteristics of the Quidel Molecular Direct C. difficile Assay were established during a prospective study conducted August to November 2012. Six hundred sixty-five (665) specimens used for this study were collected from patients suspected of having *Clostridium difficile*-associated disease (CDAD) at four distinct geographical sites across the United States. These specimens were tested with the Quidel Assay on the 7500 Fast Dx at one of three (3) facilities.

Nine specimens (1.35%) were invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. We calculated the age and gender distribution based on the initial test result obtained for each specimen. Therefore, the patient age and gender data below is for the remaining six hundred fifty-six (656) specimens.

510(k) Summary: Quidel Molecular Direct C. difficile Assay

Combined Sites – Age and Gender Distribution				
Age	Gender		Total	Prevalence by age of *C. difficile* positives with the Quidel Molecular Direct C. difficile Assay on the Applied Biosystems 7500 Fast Dx
	Male	Female		
Unknown Gender			3	33.3% (1/3)
Infant (<2 years)	4	4	8	12.5% (1/8)
Child (≥2 to <12 years)	21	18	39	25.6% (10/39)
Adolescent (≥12 to <18 years)	8	11	19	21.1% (4/19)
Transitional Adolescent (≥18 to ≤21 years)	5	8	13	15.4% (2/13)
Adult (>21 to 59 years)	132	146	278	19.1% (53/278)
Sr. Adult (≥ 60 years)	127	169	296	15.9% (47/296)
Total	297	356	656	18.0% (118/656)

Direct Culture Cytotoxicity Assay Comparison

Six hundred sixty-five specimens were tested by both the Quidel Molecular Direct C. difficile Assay and the tissue culture cytotoxin assay. Three specimens (0.5%) were indeterminate in the cytotoxin assay due to toxicity in the antitoxin well. Nine specimens (1.35%) were invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. Eight specimens yielded a valid result when retested according to the Quidel Molecular Direct C. difficile Assay draft package insert (7 were negative, 1 was positive). One specimen remained invalid upon repeat testing. We calculated clinical performance based on the initial test result obtained for each specimen. Therefore, the data below is for the remaining six hundred fifty-three (653) specimens.

Combined Sites – Combined Ages								
	Direct Culture						**95% CI**	
Quidel Molecular Real-Time PCR Direct C. difficile Assay on ABI 7500		**POS**	**NEG**	**Total**	**Sensitivity**	**94.3%**	**87.4%**	**97.5%**
	POS	**83**	**33***	**116**	**Specificity**	**94.2%**	**91.9%**	**95.8%**
	NEG	**5****	**532**	**537**				
	Total	**88**	**565**	**653**				

510(k) Summary: Quidel Molecular Direct C. difficile Assay

* Of the thirty-three (33) discordant specimens (Quidel Molecular Positive/Direct Culture Negative) reported, thirty-two (32) were tested with a FDA-cleared molecular device. All thirty-two of these specimens were positive for *C. difficile*. The remaining specimen was unavailable for testing.

** Five (5) discordant specimens (Quidel Negative/Tissue Culture Cytotoxin Positive) reported were tested with the FDA-cleared molecular device. All five (5) of these specimens were found to be negative for *C. difficile*.

Enriched Toxigenic Culture Comparison

Six hundred sixty-five (665) specimens were tested by both the Quidel Molecular Direct C. difficile Assay and enriched toxigenic culture. Nine specimens (1.35%) were invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. Eight specimens yielded a valid result (7 were negative, 1 was positive) when retested according to the Quidel Molecular Direct C. difficile Assay draft package insert. One specimen remained invalid upon repeat testing. We calculated clinical performance based on the initial test result obtained for each specimen. Therefore, the data below is for the remaining six hundred fifty-six (656) specimens.

Combined Sites – Combined Ages								
Enhanced Toxigenic Culture							**95% CI**	
Quidel Molecular Direct C. difficile Assay on ABI 7500		**POS**	**NEG**	**Total**	**Sensitivity**	**88.9%**	**82.2%**	**93.3%**
	POS	**112**	**6***	**118**	**Specificity**	**98.9%**	**97.6%**	**99.5%**
	NEG	**14****	**524**	**538**				
	Total	**126**	**530**	**656**				

* Six (6) discordant specimens (Quidel Molecular Positive/Enriched Toxigenic Culture Negative) reported were tested with a FDA-cleared molecular device. All of these specimens were positive for *C. difficile*.

** Twelve (12) discordant specimens (Quidel Negative/ Enriched Toxigenic Culture Positive) reported in Table 20.15, were tested with a FDA-cleared molecular device. Two (2) specimens were unavailable for testing. Nine (9) of these specimens were found negative for *C. difficile*, and three (3) were positive.

Life Technologies QuantStudio Dx Real-Time PCR Instrument System

Performance characteristics of the Quidel Molecular Direct C. difficile Assay were established during a prospective study conducted August to November 2012. Seven hundred ninety-two (792) samples used for this study were collected from patients suspected of having *Clostridium difficile*-associated disease (CDAD) at four (4) distinct geographical sites across the United States. These specimens were tested with the Quidel Assay on the QuantStudio Dx Instrument at one of three (3) facilities.

One (1) specimen (0.1%) was invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. We calculated age and gender distribution based on the initial test result obtained for each specimen. Therefore, the patient age and gender data below is for the remaining seven hundred ninety-one (791) specimens.

Combined Sites – Age and Gender Distribution				
Age	Gender		Total	Prevalence by age of *C. difficile* positives with the Quidel Molecular Direct C. difficile Assay on the QuantStudio
	Male	Female		
Unknown Gender			2	50.0% (1/2)
Infant (<2 years)	5	5	10	10.0% (1/10)
Child (≥2 to <12 years)	28	21	49	24.5% (12/49)
Adolescent (≥12 to <18 years)	10	14	24	20.8% (5/24)
Transitional Adolescent (≥18 to ≤21 years)	6	7	13	7.7% (1/13)
Adult (>21 to 59 years)	158	170	328	18.3% (60/328)
Sr. Adult (≥ 60 years)	163	202	365	17.8% (65/365)
Total	370	419	791	18.3% (145/791)

Direct Culture Assay Comparison

Seven hundred and ninety-two samples were tested by both the Quidel Molecular Direct C. difficile Assay and the direct culture assay. Three (3) specimens (0.4%) were indeterminate in the cytotoxin assay due to toxicity in the antitoxin well. One (1) specimen (0.1%) was invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. The specimen yielded a valid result when retested according to the Quidel Molecular Direct C. difficile Assay draft package insert (it was negative). We calculated clinical performance based on the initial test result obtained for each specimen. Therefore, the data below is for the remaining seven hundred eighty-eight (788) specimens.

Combined Sites – Combined Ages								
	Tissue Culture Cytotoxin						95% CI	
Quidel Molecular Direct C. difficile Assay on LTI QuantStudio		POS	NEG	Total	Sensitivity	93.3%	86.9%	96.7%
	POS	98	45*	143	Specificity	93.4%	91.3%	95.0%
	NEG	7**	638	645				
	Total	105	683	788				

* Of the forty-five (45) discordant specimens (Quidel Molecular Positive/Direct Culture Negative) reported, forty-four (44) were tested with a FDA-cleared molecular device. Thirty-five (35) of these specimens were positive for *C. difficile*, and nine (9) were negative. The remaining specimen was unavailable for testing.

** Seven (7) discordant specimens (Quidel Negative/Direct Culture Positive) reported were tested with a FDA-cleared molecular device. Two (2) of these specimens were found positive for *C. difficile*, and five (5) were negative.

Enriched Toxigenic Culture Comparison

Seven hundred ninety-two (792) samples were tested by both the Quidel Molecular Direct C. difficile Assay and enhanced toxigenic culture. One (1) specimen (0.1%) was invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. The specimen yielded a valid result (it was negative) when retested according to the Quidel Molecular Direct C. difficile Assay draft package insert. We elected to calculate clinical performance based on the initial test result obtained for each specimen. Therefore, the data below is for the remaining seven hundred ninety-one (791) specimens.

Combined Sites – Combined Ages								
	Enriched Toxigenic Culture						95% CI	
Quidel Molecular Direct C. difficile Assay on LTI QuantStudio		POS	NEG	Total	Sensitivity	87.3%	81.1%	91.6%
	POS	137	8*	145	Specificity	98.7%	97.5%	99.4%
	NEG	20**	626	646				
	Total	157	634	791				

* Eight (8) discordant specimens (Quidel Molecular Positive/Enriched Toxigenic Culture Negative) reported were tested with a FDA-cleared molecular device. Two (2) of these specimens were positive for *C. difficile*, and six (6) were negative.

** Seventeen (17) out of twenty (20) discordant specimens (Quidel Negative/ Enriched Toxigenic Culture Positive) reported, were tested with a FDA-cleared molecular device. Three (3) specimens were unavailable for testing. Eleven (11) of these specimens were found negative for *C. difficile*, and six (6) were positive.

Cepheid SmartCycler II

Performance characteristics of the Quidel Molecular Direct C. difficile Assay were established during a prospective study conducted August to November 2012. Six hundred sixty-five (665) specimens used for this study were collected from patients suspected of having *Clostridium difficile*-associated disease (CDAD) at four distinct geographical sites across the United States. These specimens were tested with the Quidel Assay on the SmartCycler II at one of three (3) facilities.

Five (5) specimens (0.75%) were invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. We calculated the age and gender distribution based on the initial test result obtained for each specimen. Therefore, the patient age and gender data below is for the remaining six hundred sixty (660) specimens.

Combined Sites – Age and Gender Distribution				
Age	Gender		Total	Prevalence by age of *C. difficile* positives with the Quidel Molecular Direct C. difficile Assay on the Cepheid SmartCycler II
	M	F		
Unknown Gender			3	33.3% (1/3)
Infant (<2 years)	4	4	8	12.5% (1/8)
Child (≥2 to <12 years)	21	18	39	23.1% (9/39)
Adolescent (≥12 to <18 years)	8	11	19	15.8% (3/19)
Transitional Adolescent (≥18 to ≤21 years)	5	8	13	7.7% (1/13)
Adult (>21 to 59 years)	133	147	280	18.6% (52/280)
Sr. Adult (≥ 60 years)	129	169	298	17.1% (51/298)
Total	300	357	660	17.9% (118/660)

Direct Culture Assay Comparison

Six hundred sixty-five specimens were tested by both the Quidel Molecular Direct C. difficile Assay and the direct culture assay. Three (3) specimens (0.5%) were indeterminate in the cytotoxin assay due to toxicity in the antitoxin well. Five (5) specimens (0.75%) were invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. All five (5) specimens yielded a valid when retested according to the Quidel Molecular Direct C. difficile Assay draft package insert result (3 were negative, 2 were positive). We calculated clinical performance based on the initial test result obtained for each specimen. Therefore, the data below is for the remaining six hundred fifty-seven (657) specimens.

Combined Sites – Combined Ages								
Tissue Culture Cytotoxin							95% CI	
Quidel Molecular Direct C. difficile Assay on Cepheid SmartCycler II		POS	NEG	Total	Sensitivity	89.7%	81.5%	94.5%
	POS	78	38*	116	Specificity	93.3%	91.0%	95.1%
	NEG	9**	532	541				
	Total	87	570	657				

* The thirty-three (38) discordant specimens (Quidel Molecular Positive/Direct Culture Negative) reported were tested with a FDA-cleared molecular device. Nine (9) of these specimens were negative for *C. difficile*, and twenty-nine (29) were positive for *C. difficile*.

** Eight (8) of the nine (9) discordant specimens (Quidel Negative/Direct Culture Positive) reported were tested with a FDA-cleared molecular device. One (1) specimen was unavailable for testing. Five (5) of these specimens were found to be negative for *C. difficile*, and three (3) were found to be positive.

Enriched Toxigenic Culture Comparison

Six hundred sixty-five (665) specimens were tested by both the Quidel Molecular Direct C. difficile Assay and enriched toxigenic culture. Five (5) specimens (0.75%) were invalid in the Quidel Molecular Direct C. difficile Assay when initially tested. All five (5) specimens yielded a valid result when retested according to the Quidel Molecular Direct C. difficile (3 were negative, 2 were positive). We elected to calculate clinical performance based on the initial test result obtained for each specimen. Therefore, the data below is for the remaining six hundred sixty (660) specimens.

510(k) Summary: Quidel Molecular Direct C. difficile Assay

Combined Sites – Combined Ages								
Enhanced Toxigenic Culture							95% CI	
Quidel Molecular Direct C. difficile Assay on Cepheid SmartCycler II		POS	NEG	Total	Sensitivity	82.4%	74.8%	88.1%
	POS	103	15*	118	Specificity	97.9%	95.4%	98.3%
	NEG	22**	520	542				
	Total	125	535	660				

* Fifteen (15) discordant specimens (Quidel Molecular Positive/Enriched Toxigenic Culture Negative) reported were tested with a FDA-cleared molecular device. Six (6) of these specimens were positive for, nine (9) of these specimens were negative.

** Nineteen (19) of the twenty-two (22) discordant specimens (Quidel Negative/ Enriched Toxigenic Culture Positive) reported were tested with a FDA-cleared molecular device. Three (3) specimens were unavailable for testing. Ten (10) of these specimens were found to be positive for *C. difficile*, and nine (9) were found to be negative.

Proposed Labeling:

The labeling is per the requirements of 21 CFR Part 809.10.

Conclusion:

Quidel has submitted this 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. This summary of 510(k) safety and effectiveness information provides the necessary detail for a determination of substantial equivalence for the Quidel Molecular Direct C. difficile Assay.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

Quidel Corporation
C/O Ronald H. Lollar
10165 McKellar Court
San Diego, California 92121

March 8, 2013

Re: K123998

Trade/Device Name:	Quidel Molecular Direct C. difficile Assay
Regulation Number:	21 CFR §866.3130
Regulation Name:	*C. difficile* Nucleic Acid Amplification Test Assay
Regulatory Class:	Class II
Product Code:	OZN, OOI
Dated:	December 20, 2012
Received:	December 26, 2012

Dear Mr. Lollar:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical

forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Sally A. Hojvat

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) NumberK123998

Device Name: Quidel Molecular Direct C. difficile Assay

Indication for Use:

The Quidel Molecular Direct C. difficile Assay is a qualitative, multiplexed *in vitro* diagnostic test for the direct detection of toxin A gene (*tcdA*) or toxin B gene (*tcdB*) sequences of toxigenic strains of *Clostridium difficile* from unformed (liquid or soft) stool specimens collected from patients suspected of having *Clostridium difficile*-Associated Disease (CDAD).

The Quidel Molecular Direct C. difficile Assay is a real-time PCR test and utilizes proprietary sample preparation with fluorescently labeled primers and probes. The assay can be performed using either the Life Technologies QuantStudio® Dx; the Applied Biosystems 7500 Fast Dx, or the Cepheid SmartCycler II, to detect the toxin gene sequences associated with toxin-producing *C. difficile* strains.

The assay is intended to be performed directly on CDAD-suspected stool specimens, and is indicated for use as an aid in the diagnosis of CDAD.

Prescription Use		Over-The-Counter Use
X	AND/OR	_____
(Part 21 CFR 801 Subpart D)		(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of Device Evaluation (ODE)

Raquel A. Peat -S
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Division Sign-Off
CDRH, Center for Devices and Radiological Health
510(k) K123998